

In the Claims:

Please cancel claims 1-22 without prejudice and add new claims 23-36 as follows:

23. (NEW) A method for providing new therapeutic agent(s), characterized in that it comprises the following steps:

a) selecting at least one polypeptide encoded by a natural allelic variant of one preselected gene with therapeutic potential;

b) determining the therapeutic index of the polypeptide(s) selected in step a) by

i) submitting the polypeptides selected in step a) to at least two activity tests;

ii) attributing a value to each polypeptide in direct relation with the results of said activity tests; and

iii) determining the therapeutic index of each polypeptide from the values attributed in step ii).

c) retaining as therapeutic agent(s), the polypeptide(s) selected in step a) whose therapeutic index, as determined in step b), is higher than a therapeutic index of reference.

24. (NEW) The method according to claim 23, wherein the therapeutic index in step b) is determined without resorting to *in vivo* activity tests.

25. (NEW) The method according to claim 23 or 24, characterized in that at least 2 polypeptides, preferably at least 4 polypeptides, are selected in step a).

26. (NEW) The method according to any one of claims 23 or 24, wherein the therapeutic index of reference is the therapeutic index of one reference product.

27. (NEW) The method according to any one of claims 23 or 24, characterized in that it further comprises a step d), wherein only the polypeptide(s) retained in step c) which has (have) the highest or second highest therapeutic index, is (are) selected as therapeutic agent(s).

28. (NEW) The method according to any one of claims 23, wherein the polypeptides selected in step a) are polypeptides encoded by natural allelic variants of one preselected gene with therapeutic potential.

29. (NEW) The method according to any one of claims 23, wherein said natural allelic variants originate from the same species.

30. (NEW) The method according to claim 29, wherein said natural allelic variants originate from the human species.

31. (NEW) The method according to any one of claims 23, 24, 28, 29, or 30, wherein the polypeptides selected in step a) are polypeptides encoded by natural allelic variants of one single gene that can be either the preselected gene with therapeutic potential or one related gene thereof.

32. (NEW) The method according to any one of claims 29 or 30, wherein the polypeptides selected in step a) are under their mature form.

33. (NEW) The method according to any one of claims 23, 24, 28, 29, or 30, wherein the amino acid sequences of the mature form of all the polypeptides selected in step a) do not differ one from each other by more than 20 amino acids, preferably by more than 10 amino acids, more preferably by only one single amino acid.

34. (NEW) The method according to any one of claims 23, 24, 28, 29, or 30, wherein said preselected gene with therapeutic potential is a gene encoding a cytokine.

35. (NEW) The method according to any one of claims 23, 24, 28, 29, or 30, wherein at least one activity test is carried out by means of a gene expression vector carrying a polynucleotide which encodes one of the polypeptides selected in step a).

36. (NEW) A therapeutic agent obtainable by the method according to any one of claims 23, 24, 28, 29, or 30.

CONCLUSION

This preliminary amendment has been filed within the time period as set forth and in accordance with 37 CFR 1.115 (b)(2)(iii).

The Applicants respectfully request expeditious consideration and allowance of the present application. The Examiner is invited and encouraged to telephone the undersigned if he believes such would facilitate furtherance of the prosecution of the present application.

Should any fee be missing or insufficient, the Commissioner is hereby authorized to charge said fee to Account No. 50-0369.

Respectfully submitted,



By: _____
John C. Serio, Reg. No. 39,023
Attorney for Applicants
Brown, Rudnick, Berlack Israels LLP
One Financial Center, Box IP
Boston, MA 02111
Customer No.: 21710
Tel: 617-856-8238
Fax: 617-856-8201
Email: ip@brownrudnick.com

Dated 5-6-05